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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte KAI-UWE LEWANDROWSKI and DEBRA TRANTOLO

Appeal 2007-2917
Application 10/054,171
Technology Center 1600

Decided: January 3, 2008

Before ERIC GRIMES, LORA M. GREEN, and
RICHARD M. LEBOVITZ, *Administrative Patent Judges*.

GRIMES, *Administrative Patent Judge*.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 involving claims to a method of detecting osteoporosis. The Examiner has rejected the claims as nonenabled and obvious. We have jurisdiction under 35 U.S.C. § 6(b). We affirm in part.

BACKGROUND

"[T]he present application relates to identifying humoral markers for bone loss on the basis of bacterial or mammalian molecular chaperones" (Spec. 1). "The term molecular chaperone describes a number of unrelated proteins that are involved in the assembly and reassembly of proteins. . . .

Some of these proteins are referred to as heat shock proteins ('HSPs') or stress proteins." (*Id.* at 5.) "By definition, HSP expression is elevated in cells undergoing stress, such as those in damaged or inflamed tissue. Conditions as diverse as a rise in temperature, hypoxia, irradiation, infection and exposure to toxic chemicals can all result in increased HSP expression." (*Id.*)

E. coli and mammalian molecular chaperones have been shown to stimulate bone resorption in a murine calvarial bone resorption assay. *See* the instant Specification, paragraph bridging pages 44-45, and Nair[1] (abstract), which is almost identical. The Specification states that bacterial endotoxin-LPS also stimulates *in vitro* bone resorption as well as "inhibit[ing] bone collagen and noncol[l]agenous protein synthesis" (Spec. 16).

The Specification discloses a "method of diagnosing osteoporosis . . . [that] includes 1) sampling the tissue or cells of a mammalian subject, 2) measuring the level of a marker and 3) designating the mammalian subject as having osteoporosis if the level of the marker is higher than a standard level of the marker in a member of a control group" (*id.* at 26-27). "The marker can be either a bacteria, a bacteria produced factor, or a chaperon[e] molecule" (*id.* at 27).

The Specification provides a working example describing a comparison of proteins in bone samples from "healthy and compromised subjects" (*id.* at 50). The results reportedly show "an association between compromised bone sample[s] and electrophoretic bands in the 45-65 kDa

[1] Nair et al., "Molecular chaperones stimulate bone resorption," *Calcif. Tissue Int.*, Vol. 64, pp. 214-218 (1999).

region" (*id.* at 51). The Specification provides a prophetic example describing comparison of molecular chaperones in healthy and osteoporotic samples (*id.* at 51-55).

DISCUSSION

1. CLAIMS

Claims 1-6, 8, 10-14, and 19 are on appeal. The Examiner has indicated that claims 7, 9, and 15-18 would be allowable if rewritten in independent form (Answer 7).

The claims have not been argued separately and therefore stand or fall together. 37 C.F.R. § 41.37(c)(1)(vii). Claim 1 is the only independent claim and reads as follows:

1. A method of detecting osteoporosis in a individual to be tested comprising:

a) obtaining a sample of a bone related tissue or cells; and

b) assaying the concentration of at least one marker selected from the group consisting of infectious agents, a factor produced by an infectious agent, and heat shock proteins (HSPs) produced in response to an infectious agent, and

c) comparing the concentration of the at least one marker with the concentration of the marker in a sample of the same bone related tissue or cells from a control individual who does not have osteoporosis.

2. ENABLEMENT

Claims 1, 2, 12, and 13 stand rejected under 35 U.S.C. § 112, first paragraph, on the basis that the Specification, "while being enabling for detection of osteoporosis caused by bacterial infection, does not reasonably provide enablement for detecting osteoporosis by measuring concentration of other types of pathogens such as viruses, [etc.], as recited in instant claims

12, and 13" (Answer 3).[2] The Examiner concludes that undue experimentation would be required to practice the claimed method because "the scope of the claims is broader than the disclosure in the specification. The efficacy of the invention is unpredictable because of the wide variety of pathogens known to a skilled artisan. No direction or guidance, or working example is given by the inventors with respect to the recited pathogens in claims 12 and 13" (*id.* at 4).

We agree with the Examiner that the Specification does not provide an enabling disclosure with respect to pathogens other than bacteria. It is well-settled that a

> specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented *must* be taken as in compliance with the enabling requirement of the first paragraph of § 112 *unless* there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support.

In re Marzocchi, 439 F.2d 220, 223 (CCPA 1971).

In this case, however, the Specification does not disclose that osteoporosis can be detected by assaying for pathogens other than bacteria. For example, the "Summary of the Invention" is of a "method of detecting osteoporosis . . . [by] measuring the concentration of at least a marker which is one of bacteria, bacteria produced factors, or heat shock proteins (HSPs)" (Spec. 3-4). Likewise, the section of the Specification discussing diagnosis is headed "Diagnosing Osteoporosis using Bacterial and/or Molecular

[2] The statement of the rejection in the Examiner's Answer includes claims 1-19, but the Examiner later clarified that claims 3-11 and 14-19 were not intended to be included (Answer 7).

Chaperone Markers" (*id.* at 26) and states that the "marker can be either a bacteria, a bacteria produced factor, or a chaperon[e] molecule" (*id.* at 27). Although one section of the Specification is headed "Identification of Bacterial or Viral Markers for Osteoporosis" (Spec. 14), that section discusses only bacterial markers and molecular chaperones; no viral markers are disclosed.

In terms of the factors set out in *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988), the Specification provides no guidance or working examples to aid those skilled in the art in detecting osteoporosis by assaying for pathogens other than bacteria. The state of the prior art does not aid in reducing the amount of experimentation because the evidence of record does not show that those skilled in the art recognized a correlation between osteoporosis and pathogens other than bacteria. The scope of the claims is very broad and the evidence of record provides no basis for those skilled in the art to predict which pathogens will or will not be associated with osteoporosis. On the other hand, the level of skill in the art is high. On balance, however, the *Wands* factors support the Examiner's conclusion that undue experimentation would be required to practice the full scope of the rejected claims.

Appellants argue that they "have described the known association of certain parasites and protozoans with bone disease (See [Specification] page 34) and the association of a number of viruses with production of HSPs (pages 39-40; 31-32)" (Appeal Br. 9).

We have reviewed the cited pages of the Specification but do not agree that they provide the requisite guidance. Page 34 of the Specification

is part of a discussion of treating or preventing, not diagnosing, osteoporosis. In addition, that page states that "[o]steoporosis caused by infectious diseases of bone that can be diagnosed using a chaperon[e] molecule marker can be caused by . . . viruses, bacteria, fungi, protozoa, and parasites" (*id.* at 34, ll. 17-18). Although that passage refers to "[o]steoporosis caused by infectious diseases . . . caused by" various agents, it states that the osteoporosis is "diagnosed using a chaperon[e] molecule marker" not a marker derived from the infectious agent.

Pages 31-32 and 39-40 of the Specification are also unhelpful to Appellants' position. Pages 31-32 are again concerned with treatment or prevention, not diagnosis, and the viruses recited are disclosed as sources of "[i]mmunogenic or antigenic peptides that are endogenously complexed to HSPs or MHC antigens" to be used in treatment or prevention. Pages 39-40 are part of a discussion of inducing resistance to osteoporosis by immunization and do not include any disclosure of diagnosing osteoporosis based on markers from non-bacterial pathogens.

Appellants also argue that the type of experimentation required to obtain bone related samples and assay them for markers is routine (Appeal Br. 10-11).

It is true that the type of experimentation required is a factor in determining enablement. *See Wands*, 858 F.2d at 737 (Some experimentation, even a considerable amount, is not "undue" if, e.g., it is merely routine). However, the experimentation required to practice the full scope of the instant claims requires more than simply choosing a known marker, assaying for it, and comparing the result to a standard. The instant

claims also require determining whether a given marker is correlated with osteoporosis in the first place.

The Specification provides absolutely no guidance regarding which markers from which non-bacterial pathogens are and are not associated with osteoporosis. "Tossing out the mere germ of an idea does not constitute enabling disclosure. While every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention." *Genentech Inc. v. Novo Nordisk A/S*, 108 F.3d 1361, 1366 (Fed. Cir. 1997). The routine nature of obtaining a sample and assaying for a given marker, once it has been shown to be associated with osteoporosis, is not enough to make up for the Specification's complete lack of guidance regarding diagnosing osteoporosis based on markers from non-bacterial pathogens.

Finally, Appellants argue that the Examiner's reliance on Nair "as evidence to question the adequacy of the disclosure to enable the claims is flawed" (Reply Br. 3) for several reasons (*id.* at 3-5).

We agree with Appellants that Nair relates only to bacterial HSPs and shows that each of the three tested *E. coli* HSPs stimulated bone resorption. The Examiner, however, has indicated that the claims are enabled with respect to diagnosing osteoporosis based on bacteria or bacterial markers (Answer 3). Thus, while Nair may not provide further support for the Examiner's rejection, it provides no evidence contrary to the Examiner's position.

The Examiner's rejection is supported by a preponderance of the evidence of record. We therefore affirm the rejection of claims 1, 2, 12, and 13 under 35 U.S.C. § 112, first paragraph, for lack of enablement.

3. OBVIOUSNESS OVER FINDLAY AND NAIR

Claims 1-6, 8, 10,[3] and 11 stand rejected under 35 U.S.C. § 103(a) as obvious in view of Findlay[4] and Nair. The Examiner finds that "Findlay teaches the method of diagnosing osteroporosis [sic] or osteroarthritis [sic] by detecting biochemical markers . . . using markers associated with bone resorption, [but] fails to teach using the pathogens or heat shock proteins" recited in claim 1. (Answer 5.) The Examiner relies on Nair for teaching that "molecular chaperones (heat shock proteins) stimulate bone resorption" (*id.*). The Examiner concludes that

> [g]iven the general teaching in Findl[a]y that the method of detection of osteoporosis by screening the concentration of markers associated with bone resorption, it would have been obvious to one having ordinary skill in the art at the time the invention was made to have looked to the prior arts such as Nair for specific types of markers that also stimulate bone resorption.

(*Id.* at 6.)

We agree with the Examiner that the method of claim 1 would have been obvious to a person of ordinary skill in the art in view of Findlay and Nair. Findlay teaches that osteoporosis "is a bone disorder whereby the bone balance of remodeling is skewed in the favour of bone loss" (Findlay

[3] Claim 10 is not included in the statement of either § 103 rejection in the Examiner's Answer but the Examiner made clear that claim 10 was included in the rejections (Answer 7). Appellants recognized that the rejections include claim 10 (Reply Br. 2).

[4] Findlay et al., WO 00/13024, March 9, 2000.

6: 22-23). Findlay teaches that patients susceptible to osteoporosis can be identified by "taking a sample of body tissue or body fluid and measuring or estimating the level of at least one regulator or marker of bone remodeling in the sample" (*id.* at 3: 32-33). "The body tissue sampled may be bone" (*id.* at 4: 5). The regulator or marker can be one associated with bone resorption or formation or an inhibitor of bone resorption (*id.* at 4: 21-32).

The markers disclosed by Findlay do not include heat shock proteins or molecular chaperones. However, Nair teaches that all three *E. coli* HSPs tested and three out of four tested mammalian HSPs stimulated bone resorption in an *in vitro* assay (Nair, abstract). Nair concludes that the "finding that mammalian molecular chaperones can also induce calvarial breakdown raises the possibility that release of these proteins from bone cells could cause bone pathology in conditions not involving bacterial infection" (*id.* at 218).

We agree with the Examiner that it would have been obvious to a person of ordinary skill in the art to measure the mammalian molecular chaperones disclosed by Nair (HSPs with molecular weights of 27, 70, and 90 kDa) in Findlay's method of detecting osteoporosis, because Findlay teaches that markers useful in the disclosed method include those associated with bone resorption and Nair teaches that HSP 27, HSP 70 and HSP 90 all induce bone resorption. The method made obvious by Findlay and Nair meets all the limitations of instant claim 1.

Appellants argue that Findlay and Nair do not disclose or suggest a method of detecting osteoporosis by "measuring endogenous factors, such as heat shock proteins, that are **induced by infection**" (App. Br. 14).

Appellants also argue that "Findlay and Nair do not disclose, suggest or provide one of ordinary skill in the art with a reasonable expectation of success that assaying the concentration of . . . **endogenous** factors that are altered in expression **due to an infectious agent** in bone related tissue or cells can be used to detect osteoporosis" (*id.* at 15).

This argument is not persuasive. The instant Specification states that the expression of heat shock proteins is "[b]y definition" elevated in response to stress, including stress resulting from infection (Specification 5). In addition, the 70 kDa and 90 kDa heat shock proteins disclosed by Nair to stimulate bone resorption reasonably appear to be the same as the "HSP 70" and "HSP 90" proteins recited in, for example, claim 4. *See* Nair, page 217, right-hand column ("bovine hsp 70, and human hsp 90 . . . were able to stimulate bone resorption"). Appellants have provided no evidence to show that Nair's heat shock proteins are not "produced in response to an infectious agent," as recited in claim 1.

Thus, a preponderance of the evidence in the record supports the Examiner's position that the method made obvious by the cited references meets the limitations of instant claim 1. The rejection of claim 1 is affirmed. Claims 2-6, 8, 10, and 11 fall with claim 1.

4. OBVIOUSNESS OVER FINDLAY AND REDDI

Claims 1, 10, 12-14, and 19 stand rejected under 35 U.S.C. § 103(a) as obvious in view of Findlay and Reddi.[5] The Examiner relies on Findlay

[5] Reddi et al., "The *Escherichia coli* chaperonin 60 (groEL) is a potent stimulator of osteoclast formation," *Journal of Bone and Mineral Research*, Vol. 13, pp. 1260-1266 (1998).

for the disclosure discussed above. The Examiner cites Reddi as teaching that

> the E. coli chaperonin 60 (groEL) stimulates bone resorption and osteoclast formation. See abstract. The reference suggests that bacterial cpn60s may play a role in the osteolysis associated with bone infections. . . . The reference suggests the possibility that bacterial infection of the chaperonins could be responsible for bone infection diseases such as osteoporosis.

(Answer 6.)

Appellants argue that "Reddi does not relate to osteoporosis. . . . Even Reddi acknowledges that his studies are distinct from studies involving osteoporosis, noting in the abstract 'Whether endogenous ("self") chaperonins have a role in other bone loss disorde[r]s, such as osteoporosis, is an intriguing possibility'." (App. Br. 16-17.)

We will reverse this rejection. Reddi teaches that *E. coli* chaperonin 60 (cpn60 or groEL) stimulates bone resorption (Reddi, abstract). However, Reddi does not teach any relationship between groEL and osteoporosis, suggesting only that "the potent bone-resorbing activity of certain bacterial chaperonins suggest that these proteins play a role in the bone damage that accompanies infection" (*id.* at 1265). Osteoporosis, however, is not infection. *See id.* ("[E]ukaryotic molecular chaperones could have pathological roles in *idiopathic* conditions such as osteoporosis" (emphasis added)).

The rejection of claims 1, 10, 12-14, and 19 as obvious over Findlay and Reddi is reversed.

SUMMARY

We affirm the rejection of claims 1, 2, 12, and 13 as nonenabled and the rejection of claims 1-6, 8, 10, and 11 as obvious in view of Findlay and Nair. However, we reverse the rejection of claims 1, 10, 12-14, and 19 as obvious in view of Findlay and Reddi.

AFFIRMED-IN-PART

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